Amendments to the Specification:

Please replace the section beginning at page 1, line 2 with the following redlined section:

~~CROSS REFERENCE TO RELATED APPLICATIONS~~

~~This application is a Continuation-in-Part of~~ U.S. Ser. No. 10/053,530~~, filed Jan. 17, 2002, which is incorporated herein by reference in its entirety and which claims the benefit of priority of~~ U.S. Provisional Application Ser. Nos. 60/367,358~~ (formerly U.S. Ser. No. 09/765,208, filed Jan. 17, 2001), also incorporated herein by reference in its entirety and for which a Petition to Convert a Non-Provisional Application to a Provisional Application was filed on Jan. 16, 2002, and granted on Jun. 6, 2002. This application also claims the benefit of priority of~~ and ~~U.S. Provisional Application No.~~ 60/385,691~~ filed on Jun. 3, 2002, and entitled "Recombinant Signaling Receptors for Tumor Gene Therapy," which is also~~ are incorporated herein by reference in ~~its~~ their entirety.

Please insert the following new section immediately before the section entitled "Field of the Invention" at page 1, line 13:

STATEMENT REGARDING SEQUENCE LISTING

The Sequence Listing associated with this application is provided in text format in lieu of a paper copy, and is hereby incorporated by reference into the specification. The name of the text file containing the Sequence Listing is 910180_401C2_SEQUENCE_LISTING.txt. The text file is 1293 KB, was created on February 18, 2009, and is being submitted electronically via EFS-Web, concurrent with the filing of the specification.

Please replace the paragraph beginning at page 66, line 3 with the following redlined section:

Specific connecting regions useful in molecules of the invention described and claimed herein include, for example, the following 18 amino acid sequences, DQEPKSCDKTHTCPPCPA (SEQ ID NO:10), DQEPKSSDKTHTSPPSPA (SEQ ID NO:18),

and DLEPKSCDKTHTCPPCPA (SEQ ID NO:12). Other specific connecting regions include, for example, the mutant hinges within the sequences referred to herein as "2H7 scFv (SSS-S)H WCH2 WCH3" and "2H7 scFv (CSS)H WCH2 WCH3", and the human IgA-derived hinge referred to herein as "2H7 scFv IgAH WCH2 WCH3".

Please replace the paragraph beginning at page 125, line 6 with the following redlined section:

The preparation of single polypeptide chain binding molecules of the Fv region, single-chain Fv molecules, is known in the art. See, *e.g.*, U.S. Pat. No. 4,946,778. In the present invention, single-chain Fv-like molecules that may be included in constructs of the invention may be synthesized by encoding a first variable region of the heavy or light chain, followed by one or more linkers to the variable region of the corresponding light or heavy chain, respectively. The selection of various appropriate linker(s) between the two variable regions is described in U.S. Pat. No. 4,946,778 (see also, *e.g.*, Huston *et al.*, 1993 *Int. Rev. Immunol.* **10**: 195). An exemplary linker described herein is $(Gly\text{-}Gly\text{-}Gly\text{-}Gly\text{-}Ser)_3$ (SEQ ID NO:529), but may be of any desired length. The linker is used to convert the naturally aggregated but chemically separate heavy and light chains into the amino terminal antigen binding portion of a single polypeptide chain, for example, wherein this antigen binding portion will fold into a structure similar to the original structure made of two polypeptide chains, or that otherwise has the ability to bind to a target, for example a target antigen. For those constructs that include an scFv as a binding region, a native or engineered immunoglobulin hinge as a connecting region, and one or more native or engineered heavy chain constant regions as a binding region, nucleotide sequences encoding the variable regions of native or engineered heavy and light chains, joined by a sequence encoding a linker, are joined to a nucleotide sequence encoding native or engineeredantibody constant regions, as desired. The constant regions may be those that permit the resulting polypeptide to form interchain disulfide bonds to form a dimer, and which contain desired effector functions, such as the ability to mediate ADCC, CDC, or fix complement, although native or engineered constant regions that do not favor dimer or other multimer fomation or aggregation are preferred. For a construct, such as an immunoglobulin-like molecule, of the invention that is intended for use in humans, the included sequences having constant regions and/or desired constant regions

function(s) will typically be human or substantially human or humanized to minimize a potential anti-human immune response and to provide appropriate or desired effector functions. Manipulation of sequences encoding antibody constant regions is referenced in the PCT publication of Morrison and Oi, WO 89/07142. In preferred embodiments, the CH1 domain is deleted in whole or in part from a tail region that includes, or consists essentially of, or consists of, a native or engineered immunoglobulin constant region(s) (for example, native or engineered CH2 and/or CH3 constant region(s), or native or engineered CH2 and/or CH3 and/or CH4 constant region(s)), and the carboxyl end of the binding region, for example, a binding domain polypeptide such as an immunoglobulin variable region polypeptide, is joined to the amino terminus of, for example, a CH2 via a connecting region, for example, a native or engineered hinge region polypeptide as provided herein.

Please replace the paragraph beginning at page 201, line 20 with the following redlined section:

Two CTLA-4 IgG fusion proteins were constructed. One fusion protein comprises the extracellular domain of CTLA-4 fused to human IgG1 wild type hinge, CH2, and CH3 domains and is designated CTLA-4 IgG WTH (CCC) WTCH2CH3 (SEQ ID NO: 78). A pD18 mammalian expression vector comprising a polynucleotide sequence encoding CTLA-4 IgG WTH (CCC) WTCH2CH3 (SEQ ID NO: 77) was prepared by fusing in frame the nucleotide sequence encoding the extracellular domain of CTLA-4 (SEQ ID NO: 83) (see U.S. Pat. No. 5,844,095) to the nucleotide sequence encoding IgG WTH (CCC) WTCH2CH3 (SEQ ID NO: 1) according to the methods described in Examples 1 and 10. The extracellular domain nucleotide sequence also comprises a BclI restriction enzyme site at the 3' end, and a leader peptide nucleotide sequence (SEQ ID NO: 79) that encodes an oncoM leader peptide (SEQ ID NO: 80). A second CTLA-4 IgG fusion protein, designated CTLA-4 IgG MTH (SSS) MTCH2WTCH3, contained the extracellular domain of CTLA-4 (plus the oncoM leader peptide sequence) fused to a mutant IgG hinge in which all three cysteine residues were replaced with serine residues. The hinge region was fused to a mutant IgG1 CH2 domain that had a mutation at isotype position 238 (EU numbering, Ward et al., supra, (position 251 using numbering according to Kabat *et al.*, *supra*; position 209 where numbering commences with first residue of IgG1 CH1;

i.e., PAPELLDGPS (SEQ ID NO: ~~1~~566) of wild type IgG1 CH2 is modified to PAPELLDGSS (SEQ ID NO: ~~1~~567)), which was fused to IgG1 wild type CH3 (U.S. Pat. No. 5,844,095). The CTLA-4 IgG MTH (SSS) MTCH2WTCH3 polynucleotide comprises the nucleotide sequence in SEQ ID NO: 85 and the deduced amino acid sequence comprises the sequence provided in SEQ ID NO: 86. CTLA-4 fusion proteins were also prepared using CTLA-4 extracellular membrane encoding sequences without the leader peptide (SEQ ID NO: 84).

Please replace the paragraph beginning at page 209, line 14 with the following redlined section:

A 2H7 scFv IgG fusion protein was constructed with the third cysteine residue in the IgG1 hinge region substituted with a serine residue. The template for introduction of the mutations was a polynucleotide encoding 2H7 scFv WTH WTCH2CH3 (SEQ ID NO: 28). The oligonucleotide introducing the mutations was a 5' PCR primer oligonucleotide HIgGMHcys3 having the sequence 5'-gtt gtt gat cag gag ccc aaa tct tgt gac aaa act cac aca tgt cca ccg tcc cca gca cct-3' (SEQ ID NO:573). The oligonucleotide introducing the mutation into the hinge region was combined with template and a 3' oligonucleotide containing an XbaI site (underlined and italicized) (5'-gtt gtt *tct aga* tca ttt acc cgg aga cag gga gag gct ctt ctg cgt gta g-3' (SEQ ID NO: 574)) to amplify the mutant hinge-wild type (WT)-CH2-CH3 sequences by PCR. The IgG MTH CCS mutant sequence was amplified for 30 cycles with a denaturation profile of 94° C, annealing at 50° C for 30 seconds, and extension at 72° C for 30 seconds. The amplified polynucleotides were inserted into the TOPO® cloning vector (Invitrogen Life Technologies) and then were sequenced as described in Example 1 to confirm the presence of the mutation. pD18 vector containing 2H7 scFv was digested to remove the constant region sequences essentially as described in Example 10. The mutant hinge-wild type CH2-CH3 regions were inserted in frame into the digested vector DNA to obtain vectors comprising 2H7 scFv MTH (CCS) WTCH2CH3 encoding DNA (SEQ ID NO: 167). The deduced polypeptide sequence is shown in SEQ ID NO: 168.

Please replace the paragraph beginning at page 218, line 10 with the following redlined section:

cDNA was anchor-tailed using terminal transferase and dGTP. PCR was then performed using an anchor-tail complementary primer and a primer that annealed specifically to the antisense strand of the constant region of either mouse Ck (for amplifcation of VL) or the appropriate isotype mouse CH1 (for amplification of VH). The amplified variable region fragments were TOPO® cloned (Invitrogen Life Technologies), and clones with inserts of the correct size were then sequenced. Consensus sequence for each variable domain was determined from sequence of at least four independent clones. The 5B9 V_L and V_H polynucleotide sequences are shown in SEQ ID NOs: 120 and 116, respectively, and the deduced amino acid sequences are shown in SEQ ID NOs: 121 and 118. The scFv was constructed by a sewing PCR method using overlapping primers containing a synthetic $(gly_4ser)_3$ (SEQ ID NO:529) linker domain inserted between the light and heavy chain variable regions (see Example 1). The 5B9 scFv polypeptide (SEQ ID NO: 123) is encoded by the polynucleotide sequence comprising SEQ ID NO: 122.

Please replace the paragraph beginning at page 245, line 16 with the following redlined section:

PCR product cloned into TOPO vector and sequenced. This product was used as the template in the second PCR reaction. Primers for the second PCR reaction:

5' primer: 5'ccgtctctgatcaggagcccaaatcttctgacaaaactcacacatccccaccgtccccagc-3' (SEQ ID NO ~~638~~637)

5' overlapping primer: 5'-

tccccaccgtccccagcacctgaactcctgggggg- gatcgtcagtcttcctcttccccccaaaacc-3' (SEQ ID NO 638) 3' primer: 5'-caggaaacagctatgac-3' (SEQ ID NO 628)

Please replace the paragraph beginning at page 262, line 28 with the following redlined section:

PCR of V_L domain with native leader peptide and part of glyser linker:

5' primer: 5'-gttgttaagcttgccgccatggagacagacacactcctgctatgg-3' (SEQ ID NO ~~652~~650)

3' primer: 5' gccacccgacccaccaccgcccgagccaccgccacctttgatttccagcttggtgcctcc-3' (SEQ ID NO 651)